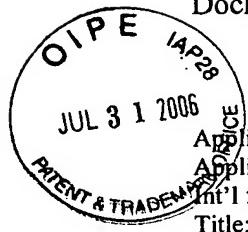


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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Stephan Ludwig, et al.  
 Application No.: 10/550,856  
 Int'l filing Date: 03/24/2004  
 Title: CASPASE INHIBITORS, ESPECIALLY CASPASE 3 INHIBITORS, FOR  
 THE TREATMENT OF INFLUENZA  
 Examiner: Unassigned  
 Group Art: Unassigned  
 Confirmation No.: 6403  
 Docket: 7003/45

## INFORMATION DISCLOSURE STATEMENT (IDS)

## MAIL STOP AMENDMENT

Commissioner For Patents  
 P.O. Box 1450  
 Alexandria, VA 22313-1450

SIR:

In accordance with 37 C.F.R. §1.56 and in compliance with 37 C.F.R. §§1.97 and 1.98, the references listed on attached Form PTO/SB/08 and/or subsequently identified herein, are being submitted herewith for consideration by the United States Patent and Trademark Office.

## I. COPIES

- a.  A legible copy of (i) each foreign patent; (ii) each publication or that portion which caused it to be listed; and (iii) all other information or that portion which caused it to be listed, is included herewith.
- b.  Any patents, publications or other information which are listed on PTO/SB/08 which are not enclosed herewith were previously cited by or submitted to the PTO in one of the following applications which has been relied upon for an earlier filing date under 35 U.S.C. §120:

U.S. Serial NumberU.S. Filing Date

## II. CONCISE EXPLANATION OF THE RELEVANCE (check at least one box)

- a.  Except as may be indicated below in (b) of this section, all of the patents, publications or other information are in the English language (concise explanation not required).
- b.  A concise explanation of the relevance of all patents, publications or other information listed that is not in the English language is as follows:
- c.  The following additional information is provided for the Examiner's consideration:

III.  CROSS REFERENCE TO RELATED APPLICATION(S)

The Examiner is advised that the following co-pending application(s) contain(s) subject matter that may be related to the present application. By bringing this (these) applications to the Examiner's attention, Applicant(s) does (do) not waive the confidentiality provisions of 35 U.S.C. §122.

Serial No.Filing DateArt Unit

FEES

- IV.  **THIS IDS IS BEING FILED UNDER 37 C.F.R. §1.97(b):** (check one box)
- a.  within three months of the filing date of a national application other than a continued prosecution application under § 1.53(d) (37 C.F.R. §1.97(b)(1)). No fee or statement is required.
- b.  within three months of the date of entry of the national stage as set forth in § 1.491 in an international application (37 C.F.R. §1.97(b)(2)). No fee or statement is required.
- c.  before the mailing date of a first Office Action on the merits (37 C.F.R. §1.97(b)(3)). No fee or statement is required.
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- a.  No statement; therefore, charge deposit account 50-1047 the fee set forth in 37 C.F.R. §1.17(p).
- b.  See the statement below. No fee is required.
- VI.  **THIS IDS IS BEING FILED UNDER 37 C.F.R. §1.97(d):**  
on or before payment of the issue fee and is accompanied by the following:
- 1) a statement under 37 C.F.R. §1.97(e) as provided below; and
- 2) charge deposit account 50-1047 the petition fee set forth in §1.17(p).
- VII.  **STATEMENT UNDER 37 C.F.R. §1.97(e) (check only one box, if applicable)**  
The undersigned hereby states that
- a.  each item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of IDS; or
- b.  no item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application, and to knowledge of the person signing the statement after making reasonable inquiry, no item of information contained in the IDS was known to any individual designated in 37 C.F.R. 1.56(c) more than three months prior to the filing of this statement, or
- c.  some of the items of information contained in the IDS were cited in a communication from a foreign Patent Office. As to this information, the undersigned states that each item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS. As to the remaining information, the undersigned hereby states that no item of this remaining information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application or, to the knowledge of the person signing the statement after making reasonable inquiry, no item of information contained in the IDS was known to any individual designated in 37 C.F.R. 1.56(c) more than three months prior to the filing of this statement.
- VIII. **PAYMENT OF FEES**
- A check in the amount of \_\_\_\_\_ is enclosed for the above-identified fee(s).
- Please charge Deposit Account No. 50-1047 in the amount of \$180.00 for the above-indicated fee(s).
- If Applicant has overlooked any additional fees, or if any overpayment has been made, the Commissioner is hereby authorized to credit or debit Deposit Account 50-1047.
- Two Copies of this paper are attached for Deposit Account charges and debits.

It is Applicant(s)'opinion that the claims presently on file patently distinguish the present invention from each of these references. The above references are being cited only in the interests of candor and without any admission that they constitute statutory prior art or contain matter which anticipates the invention or which would render the same obvious, either singly or in a combination, to a person of ordinary skill in the art.

If the Examiner has any questions concerning this IDS, he/she is requested to contact the undersigned. If it is determined that this IDS has been filed under the wrong rule, the PTO is requested to consider this IDS under the proper rule (with a petition if necessary) and charge the appropriate fee to Deposit Account No. 50-1047.

Respectfully submitted,  
Mayer & Williams PC

  
Keum J. Park  
Attorney for Applicant  
Reg. No. 42,059  
Tel. 908-518-7700

Mayer & Williams PC  
Customer Number 27774

Enclosures:  PTO/SB/08  
 References (US references omitted)  
 Search Report  
 Other:

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I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail under 37 CFR 1.8 in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on

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| Sheet  | 1 | of                     | 4                      |
|  |   | Application Number     | 10/550,856             |
|  |   | Int'l Filing Date      | 03/24/2004             |
|  |   | First Named Inventor   | Stephen Ludwig, et al. |
|  |   | Group Art Unit         | Unassigned             |
|  |   | Examiner Name          | Unassigned             |
|  |   | Attorney Docket Number | 7003/45                |

| Examiner Initials* | Cite No. <sup>1</sup> | U.S. Patent Document |                | Name of Patentee or Applicant of Cited Document | Issue Date MM-DD-YYYY |
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|   | 1.                    | HEIKE FESQ, et al., "Programmed Cell Death (Apoptosis) in Human Monocytes Infected by Influenza A Virus, <i>Immunobiol.</i> , 1994, vol. 190, pp. 175-182.  |  |  |
|   | 2.                    | ISAMU MORI, et al., "In Vivo Induction of Apoptosis by Influenza Virus", <i>Journal of General Virology</i> , 1995, vol. 76, pp. 2869-2873.   |  |  |
|   | 3.                    | TAKENORI TAKIZAWA, et. al., "Induction of Programmed Cell Death (Apoptosis) by Influenza Virus Infection In Tissue Culture Cells", <i>Journal of General Virology</i> , 1993, vol. 74, pp. 2347-2355.   |  |  |

|                    |                 |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
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|  |   |    |   | Group Art Unit         | Unassigned             |
|  |   |    |   | Examiner Name          | Unassigned             |
| Sheet  | 2 | of | 4 | Attorney Docket Number | 7003/45                |

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|   | 4.                    | HANA VAN CAMPEN, et al., "Virulent Avian Influenza A Viruses: Their Effect on Avian Lymphocytes and Macrophages <i>in vivo</i> and <i>in vitro</i> ", <i>J. Gen. Virol.</i> , 1989, vol. 70, pp. 2887-2895.  |                |
|   | 5.                    | HANA VAN CAMPEN, et al., "Destruction of Lymphocytes by a Virulent Avian Influenza A Viruses", <i>J. Gen. Virol.</i> , 1989, vol. 70, pp. 467-472.   |                |
|   | 6.                    | LARISA V. GUBAREVA, et al., "Evidence for Zanamivir Resistance in an Immunocompromised Child Infected with Influenza B Virus", <i>The Journal of Infectious Diseases</i> , 1998, vol. 178, pp. 1257-1262.  |                |
|   | 7.                    | C. SCHOLTISSEK, et al., "Failure to Obtain Drug-Resistant Variants of Influenza Virus After Treatment with Inhibiting Doses of 3-Deazaadenosine and H7", <i>Archives of Virology</i> , 1991, vol. 119, pp. 111-118.  |                |
|   | 8.                    | PHILLIP D. ZAMORE, et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals", <i>Cell</i> , March 31, 2000, vol. 101, pp. 25-33.   |                |
|   | 9.                    | YUICHI WATANABE, et al., "Role of Phosphatidylserine Exposure and Sugar Chain Desialylation at the Surface of Influenza Virus-Infected Cells in Efficient Phagocytosis by Macrophages", <i>The Journal of Biological Chemistry</i> , Issue of May 17, 2002, vol. 277, no. 20, pp. 18222-18228. |                |
|   | 10.                   | THOMAS TUSCHL, et al., Targeted mRNA Degradation by Double Stranded RNA in Vitro, downloaded from <a href="http://www.genesdev.org">www.genesdev.org</a> on April 13, 2006, pp. 3190-3197.   |                |
|   | 11.                   | TERRANCE M. TUMPEY, et al., "Depletion of Lymphocytes and Diminished Cytokine Production in Mice Infected with a Highly Virulent Influenza A (H5N1) Virus Isolated from Humans", <i>Journal of Virology</i> , July 2000, vol. 74, no. 13, pp. 6105-6116.                                       |                |

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|--------------------|-----------------|
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|  |   |    |   | Group Art Unit           | Unassigned             |
|  |   |    |   | Examiner Name            | Unassigned             |
| Sheet  | 3 | of | 4 | Attorney Docket Number   | 7003/45                |

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|   | 12.                   | NANCY A. THORNBERRY, et al., "Caspases: Enemies Within", <i>Science</i> , August 28, 1998, vol. 281, pp. 1312-1316.   |  |                |
|   | 13.                   | MUNEESH TEWARI, et al., "Yama/CPP32 $\beta$ , a Mammalian Homolog of CED-3, is a CrmA-Inhibitable Protease that Cleaves the Death Substrate Poly(ADP-Ribose) Polymerase", <i>Cell</i> , June 2, 1995, vol. 81, pp. 801-809.                                     |  |                |
|   | 14.                   | STEPHAN PLESCHKA, et al., "A Plasmid-Based Reverse Genetics System for Influenza A Virus", <i>Journal of Virology</i> , June 1996, pp. 4188-4192.   |  |                |
|   | 15.                   | STEPHAN PLESCHKA, et al., Influenza Virus Propagation is Impaired by Inhibition of the Raf/MEK/ERK Signalling Cascade", <i>Nature Cell Biology</i> , March 2001, vol. 3, 7 pages.   |  |                |
|   | 16.                   | CHRISTOPHER W. OLSEN, et al. , "bcl-2 Alters Influenza Virus Yield, Spread, and Hemagglutinin Glycosylation", <i>Journal of Virology</i> , January 1996, vol. 70, no.1, pp. 663-666.  |  |                |
|   | 17.                   | ROBERT E. O'NEILL, et al., "The Influenza Virus NEP (NS2 Protein) Mediates the Nuclear Export of Viral Ribonucleoproteins", <i>The EMBO Journal</i> , 1998, vol.17, no. 1, pp. 288-296.   |  |                |
|   | 18.                   | STEPHEN LUDWIG, et al., "Influenza Virus-Induced AP-1-Dependent Gene Expression Requires Activation of the JNK Signaling Pathway", <i>The Journal of Biological Chemistry</i> , vol. 276, no.14, issue of April 6, 2001, pp. 10990-10998.                       |  |                |
|   | 19.                   | STEPHEN LUDWIG, et al., "Influenza A Virus NS1 Protein Inhibits Activation of Jun N-Terminal Kinase and AP-1 Transcription Factors", <i>Journal of Virology</i> , vol. 76, no. 21, Nov. 2002, pp. 11166-11171.  |  |                |

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|  |   |    |   | First Named Inventor   | Stephen Ludwig, et al. |
|  |   |    |   | Group Art Unit         | Unassigned             |
|  |   |    |   | Examiner Name          | Unassigned             |
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|   | 20.                   | REINER U. JÄNICKE, et al., "Caspase-3 is Required for DNA Fragmentation and Morphological Changes Associated with Apoptosis", <i>The Journal of Biological Chemistry</i> , vol. 273, no.16, issue of April 17, 1998, pp. 9357-9360.                             |  |                |
|   | 21.                   | VIRGINIA S. HINSHAW, et al., "Apoptosis: A Mechanism of Cell Killing by Influenza A and B Viruses", <i>Journal of Virology</i> , vol. 68, no. 6, June 1994, pp. 3667-3673.  |  |                |
|   | 22.                   | LAVINA FALEIRO, et al., "Caspases Disrupt the Nuclear-Cytoplasmic Barrier", <i>The Journal of Cell Biology</i> , vol. 151, no. 5, November 27, 2000, pp. 951-959.   |  |                |
|   | 23.                   | QUINN L. DEVERAUX, et al., "X-Linked IAP is a Direct Inhibitor of Cell-Death Proteases", <i>Nature</i> , vol. 388, July 17, 1997, pp. 300-304.  |  |                |
|   | 24.                   | GERALD M. COHEN, "Caspases: The Executioners of Apoptosis", <i>Biochem J.</i> , 1997, vol. 326, pp. 1-16.   |  |                |
|   | 25.                   | WEISAN CHEN, et al., "A Novel Influenza A Virus Mitochondrial Protein That Induces Cell Death", <i>Nature Medicine</i> , December 2001, vol. 7, no.12, pp. 1306-1312.   |  |                |
|   | 26.                   | THIJN R. BRUMMELKAMP, et al., "A System for Stable Expression of Short Interfering RNA's in Mammalian Cells", <i>Science</i> , April 19, 2002, vol. 296, pp. 550-553.   |  |                |
|   | 27.                   | SIDDHARTH BALACHANDRAN, et al., "Alpha/Beta Interferons Potentiate Virus-Induced Apoptosis Through Activation of the FADD/Caspase-8 Death Signaling Pathway", <i>Journal of Virology</i> , February 2000, pp. 1513-1523.  |  |                |

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